US Pharmacopeia Council of Experts 2005-2010: Work Plans, New Revision Approaches, and Other Enhancements

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ABSTRACT

The United States Pharmacopeial Convention (the USP Convention), which meets at 5-year intervals, last convened in 2005. At that meeting, the Convention membership elected a new Council of Experts for the 2005-2010 cycle. In turn, the Council elected members of Expert Committees charged with updating and revising the *United States Pharmacopeia–National Formulary* (*USP–NF*) and developing other authoritative standards and information. As one of their final activities, Expert Committees from the 2000-2005 cycle and USP staff carefully reviewed their work from the 2000-2005 cycle and reexamined the contents of *USP–NF*. From this comprehensive inventory emerged an updated and more focused new work plan directed toward acquiring missing monographs, updating monographs (typically because of advances in analytical technologies), and attending to General Chapter work (eg, dividing the General Chapter *Chromatography* <621> into smaller chapters) during the 2005-2010 cycle. Several elements of the work plan also speak to Resolutions adopted at the March 2005 Convention (available at www.usp.org/aboutUSP/resolutions.html) and prior ones as well. Because the work plan involves new approaches that affect both General Chapters (and thus the performance of tests and procedures) and monograph specifications—as well as the function of *Pharmacopeial Forum* and the introduction of new products—USP expects the plan to have a broad impact. This article briefly reviews some of these anticipated changes, informs constituents about how they can remain updated about progress and upcoming modifications to official texts, and invites participation in the standards-setting process.

KEYWORDS: US Pharmacopeia, United States Pharmacopeia–National Formulary, USP–NF, Pharmacopeial Forum, monograph

INTRODUCTION

The goal of the US Pharmacopeia (USP) is to promote public health by establishing and disseminating officially recognized standards of quality for and authoritative information about the use of medicines and health care technologies by health professionals, patients, and consumers (further information about USP's background, organization, and activities is available at www.usp.org/aboutUSP). USP carries out this mission by, among other activities, continuous enhancements of 2 compendia, the *United States Pharmacopeia* (*USP*) and the *National Formulary* (*NF*), through publication of revisions to the texts. These revisions include addition of new text (eg, new monographs or General Chapters), changes to current text (eg, updated analytical procedures), and removal of text (eg, deletion of monographs for articles no longer available). Although the *USP* text is still in its first edition, it is now available as *USP 29* (ie, the 29th revision). Whereas the first pharmacopeia, published in 1820, contained 621 monographs (a materia medica of 221 drugs, a secondary list of 71 drugs, and an untitled section of 329 preparations and compositions),[1] *USP 29* contains more than 4000 ingredient and drug, dietary supplement, and other product monographs for therapeutic articles legally marketed in the United States. A similar pattern of enhancement has occurred for the *NF*, which first appeared in 1888 with 435 formulas and came to USP in 1975 with 1009[2]; *NF 24* contains more than 355 excipient monographs. The variation in *NF* monographs can be explained in part by the inclusion or exclusion of formulas. For example, *NF XV* (1980) included 66 pages of monographs and 127 pages of antibiotic preparations. The latter were absent in *NF XVI* (1985), which featured 91 pages of monographs. In 1995, USP placed dietary supplements in a separate section, further limiting the number of entries in *NF*. Continuous improvement arises for at least 2 reasons: (1) advances in analytical procedures, and (2) advances in the number and types of manufactured therapeutic articles.

This work was submitted on behalf of the US Pharmacopeia (USP) Council of Experts, Expert Committee Members (Table 1), USP staff listed in USP29 NF24, pp xi-xii, xvii-xix, and xx-xxii.

REVISION PROCESS

Revisions to *USP–NF* are guided by USP's Council of Experts, who are elected at the USP Convention, which meets at 5-year intervals; the last Convention occurred in March 2005. In turn, the Council elects members of Expert Committees charged with updating and revising *USP–NF*

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Table 1. Work Plans of Several Monograph Development Expert Committees of the Council of Experts, Categorized According to Whether the Monograph Is New or Is Scheduled for Updating*

Expert Committee	Chair	Scientific Liaison	Number of New Monographs to Be Developed	Number of Old Monographs to Be Revised
Monograph Development: Antibiotics	Dr S. Hanna	Dr B. Gilbert bg@usp.org	51	129
Monograph Development: Antivirals and Antimicrobials	Dr H. Tan	Dr B. Davani bd@usp.org	172	54
Monograph Development: Cardiovascular	Dr P. Keller	Dr S. Ramakrishna rst@usp.org	117	81
Monograph Development: Cough, Cold, and Analgesics	Dr T. Wozniak	Dr C. Anthony cma@usp.org	93	162
Monograph Development: Gastrointestinal, Renal, and Endocrine	Dr J. Boehlert	Dr E. Gonikberg eg@usp.org	121	36
Monograph Development: Ophthalmics, Oncology, and Dermatology	Dr E. Cohen	F. Mao fm@usp.org	126	65
Monograph Development: Psychiatrics and Psychoactives	S. Schniepp	Dr R. Ravichandran rr@usp.org	147	133
Monograph Development: Pulmonary and Steroids	M. Cutrera	Dr D. Bempong dkb@usp.org	124	161
B&B Vaccines and Virology	Dr B.D. Garfinkle	Dr T.S. Morris tsm@usp.org	NA	NA
B&B Proteins and Polysaccharides	Dr L.C. Yeoman	Dr L.N. Callahan lnc@usp.org	8	4
B&B Cell Therapy, Gene Therapy, and Tissue Engineering	Dr W. Tente (pro tem)	Dr F. Atouf fa@usp.org	6	NA
B&B Blood and Blood Products	Dr P. Ganz	Dr A. Szajek asy@usp.org	14	13
Excipient Monographs 1	Dr Z. Chowhan	C. Sheehan cxs@usp.org	50	67
Excipient Monographs 2	Dr L. Block	Dr H. Wang hw@usp.org	36†	44
Aerosols	Dr A. Hickey	Dr K. Zaidi kxz@usp.org	27	NA

*Because of the ongoing nature of monograph commissioning and revision, these numbers are subject to change and should be regarded as close approximations. For further information and to become involved in the monograph revision process, please contact the scientific liaison, or send an e-mail to stdsmonographs@usp.org. B&B indicates Biologics and Biotechnology Collaborative Group; NA, not applicable.
†Does not include adjuvants (to be determined).

and developing other authoritative standards and information. As one of their final activities, Expert Committees from the 2000-2005 cycle and USP staff carefully reviewed their work during the 2000-2005 cycle and reexamined the content of *USP–NF*. From this comprehensive inventory emerged a significantly updated and highly focused new work plan for the 2005-2010 cycle, directed toward acquiring missing monographs, updating monographs (typically because of advances in analytical technologies), and attending to General Chapter work (eg, dividing the General Chapter *Chromatography* <621> into smaller chapters). An early outcome of this inventory was the identification of and posting on the USP Web site of a list of high-priority monographs that USP is seeking for off-patent drug substances, drug products, and excipients (www.usp.org/USPNF/submitMonograph/newMon.html). Other important work of the Council's Expert Committees beyond these compendia may be considered in separate publications.

USP has a well-established process to allow revisions to *USP–NF*. For many monographs, a Sponsor will submit a Request for Revision for either a new monograph or a revision to an existing one, following processes outlined in an available *Guideline*.[3] For General Chapters, Sponsors may

also submit Requests for Revision, but more frequently new and revised General Chapters arise as a result of decisions made by the Council of Experts. After careful consideration by USP staff and involved Expert Committees, both monograph and General Chapter Requests for Revision advance, with certain exceptions (see below), through *Pharmacopeial Forum* (*PF*), USP's bimonthly journal of standards development and compendial review, to allow public review and comment before entry into official status. USP welcomes public comments on proposed standards.

Monographs: New Revision Approaches

Creation of new monographs and revision of existing ones are top priorities for USP. USP has no authority to compel submission of information to support a public monograph.[4] Instead, over the years, USP has worked diligently to gain the cooperation of those manufacturers who understand and support the importance of a public quality standard.[5] USP has developed the following ways to work with these manufacturers:

1. USP will work diligently with first-entry manufacturers to obtain monographs for consideration by the Council of Experts (see *Guideline* in reference 3, pp 1-3).
2. For second-entry manufacturers intending to market in the United States, USP will consider Requests for Revision even though the second-entry manufacturer's article is not yet legally marketed in the United States (eg, in cases where the manufacturer has not yet received US Food and Drug Administration [FDA] approval). This approach is termed *standards for articles pending approval at FDA* and is similar to tentative approval by the FDA.[6] Proposed monographs in this category will be held as not official text (*PF*) pending a positive decision from the FDA for the second-entry manufacturer to market its article in the United States.
3. USP also has developed approaches to advance monographs to the Council of Experts if they appear in other major pharmacopeias of the world.
4. USP's Monograph and Reference Standards Development Department, working with partners when possible, may conduct laboratory testing on candidate material to determine the appropriate tests, procedures, and acceptance criteria in a proposed monograph, either a new monograph or one needing updating, for consideration by the Council of Experts.
5. USP may create monographs for articles not legally marketed in the United States, providing they are (a) intended for the treatment of neglected diseases, and (b) legally marketed in a country with a stringent regulatory authority.[7] This approach is termed *standards for articles legally marketed outside the United States.* These monographs will appear on USP's Web site for public comment and not in *PF*. When final, they will be considered "authorized" but not "official" USP text and will be maintained on USP's Web site instead of appearing in *USP–NF* or its supplements. (Section 3.03, "Function," of the Rules and Procedures of the 2005-2010 Council of Experts notes that "the Council of Experts and its Expert Committees shall function to determine and approve official content of the official compendia and other authorized publications."[8] This language draws a distinction between the content of *USP* and *NF* (which under the Federal Food Drug and Cosmetic Act [FFDCA] are official compendia of the United States and thus are legally enforceable under FFDCA) and other authoritative standards and information prepared under the oversight of and approved by the Council of Experts. This terminology is consistent with USP's Constitution and Bylaws, which frequently refer to *USP* and *NF* "and other authorized publications."
6. USP will expand its development of monographs for compounded preparations, working to obtain needed information from the biomedical literature and with internal and external laboratories to develop needed stability and other quality information to allow a beyond-use date.

Monograph Work Plan

Table 1 indicates the work plans of several monograph development Expert Committees of the Council of Experts, categorized according to whether the monograph is new or is scheduled for updating. As noted above, the USP Web site lists high-priority monographs that are considered especially important(www.usp.org/USPNF/submitMonograph/newMon.html). This list is updated regularly to show recent submissions.

General Chapters Work Plan

USP 29 contains 183 General Test and Information Chapters, of which 38 are in revision in *PF*. An additional 30 are new in *PF,* and a further 38 are in development (more are anticipated), for a total of more than 250 General Chapters present, in revision, or anticipated in *USP*. A table of the General Chapters and their status appears on the USP Web site (www.usp.org/USPNF/submitMonograph/generalChapterWorkplans.html) and is updated monthly. Individual Expert Committees prioritize their work according to their own needs.

Table 2. US Pharmacopeia Department of Standards Development Group Directors*

Group	Name	Phone	E-mail
Vice President	Todd L. Cecil, PhD	(301) 816-8234	tlc@usp.org
Veterinary Drugs and Radiopharmaceuticals	Ian F. DeVeau, PhD	(301) 816-8178	ifd@usp.org
Dietary Supplements	Gabriel I. Giancaspro, PhD	(301) 816-8343	gig@usp.org
Biologics and Biotechnology	Tina S. Morris, PhD	(301) 816-8397	tsm@usp.org
General Chapters	Todd L. Cecil, PhD (acting)	(301) 816-8234	tlc@usp.org
Small Molecules and Monograph Acquisition	Karen A. Russo, PhD	(301) 816-8379	kar@usp.org
Excipients	Catherine Sheehan	(301) 816-8262	cxs@usp.org

*The mailing address for all group directors is 12601 Twinbrook Parkway, Rockville, MD 20852-1790.

Recent Line Extensions and Other Improvements

USP is attempting to make information available to a wide variety of audiences in user-friendly formats. For example, *USP–NF* soon will be offered in 3 volumes to accommodate the increasing amount of content. Also, USP is creating new publications:

1. *USP Pharmacists' Pharmacopeia* (launched in 2005)
2. *USP–NF Spanish Edition* (launched in 2005 and official January 1, 2006)
3. *USP Veterinary Compendium* (in development)
4. *USP Dietary Supplements Compendium* (in development)

For compounding pharmacists, the *USP Pharmacists' Pharmacopeia* contains both legally enforceable abridged official *USP–NF* text and authorized text of supporting information. The creation of a scientifically exact translation of *USP 29–NF 24* into Spanish has provided USP with experience that will make other translations easier to complete. USP is working to translate *USP–NF* into Russian, and other translations are planned.

Conclusion

This article summarizes the work plan of the Council of Experts Expert Committees for the 2005-2010 revision cycle. This work plan is both extensive and intensive. Further information about specific aspects of the plan may be obtained by contacting the appropriate USP Group Director (Table 2). The plan may change depending on several factors, including Expert Committee and staff resources and focus, and the number and type of public comments received in response to a particular revision proposal. At the close of the 2005-2010 cycle, the Chair of the Council of Experts will report on the work of the Council of Experts to the USP Board of Trustees and to the Convention itself. Like the previous cycle's report, this report will focus heavily on progress in the execution of the work plan described in this article.[9,10] USP looks forward to celebrating the extraordinary work of its volunteers at the 2010 Convention.

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